**FIRST DETAILED MOLECULAR CHARACTERIZATION OF A YUS (GE*01.–02) ALLELE AND DESCRIPTION OF A NOVEL GERBICH (GE*01.–03) ALLELE RESPONSIBLE FOR RARE PHENOTYPES IN THE GERBICH BLOOD GROUP SYSTEM**

Elise Gourri[1], Erwin A. Scharberg[2], Thierry Peyrard[3,4], Beat M. Frey[1], Christoph Gassner[1]

1 Department of Molecular Diagnostics and Research & Development (MOC), Blood Transfusion Service Zurich, Swiss Red Cross, Zurich-Schlieren, Switzerland

2 Red Cross Blood Service of Baden-Wuerttemberg-Hessen, Baden-Baden, Germany

3 Institut National de la Transfusion Sanguine (INTS), Département Centre National de Référence pour les Groupes Sanguins, Paris, France,

4 Laboratory of Excellence GR-Ex, 24 Boulevard du Montparnasse, Paris, France

**Background:** The Gerbich blood group system consists of 11 antigens located on glycophorin C(GPC) and D(GPD). GPD is a truncated version of GPC, and both are encoded by the same gene, GYPC.1 “Yus”, “Gerbich“ and “Leach” correspond to the rare Ge:-2,3,4, Ge:-2,-3,4 and Ge:-2,-3,-4 types, respectively. Yus lacks the high-prevalence Ge2 antigen (exon 2 deletion), and Gerbich lacks the high-prevalence Ge2 and Ge3 antigens (exon 3 deletion).
**Aim of the project:** Serological determination of blood group Gerbich phenotypes is tedious and costly, and typing reagents are commercially unavailable. Therefore, we aimed to design a reliable, rapid and cost-effective method to screen and/or confirm them at the genetic level.
**Methods:** Three unrelated patients with anti-Gerbich had been reported to Blutspende Zurich and were serologically defined as two Gerbich and one Yus phenotype by the National Immunohematology Reference Laboratory in Paris. Positional PCRs, also accounting for the high intragenic homology, allowed for an approximate location of the deletion breakpoints present in the samples. PCR amplicons covering the suspected genomic region were sequenced. Diagnostic PCRs using Sequence Specific Priming (PCR-SSP) were developed to detect the respective allelic breakpoints and the corresponding wild-type sequences. They were used to genotype three additional samples from the Red Cross Blood Service of Baden-Baden and one Gerbich sample from the SCARF exchange program. All Baden-Baden samples had anti-Gerbich, but lacked additional phenotypic information.
**Results:** All three Zurich samples were homozygous for one deletional GYPC allele, with two different molecular backgrounds. Both Gerbich phenotypes had the same “Gerbich allele”. The genomic extent of both newly observed alleles was in line with the expected phenotypes, e.g. a deletion of exon 2 (i1-40 to i2+3512) in the Yus and a deletion of exon 3 (i2-2639 to i3+863) for the Gerbich phenotype, respectively. All three Baden-Baden samples were homozygous for either one, or the other of the previously observed alleles: two samples for the “Yus allele” and one for the “Gerbich allele”. Sequencing confirmed presence of the same alleles as previously found in the Zurich samples. The SCARF sample was unambiguously recognized as Gerbich by our PCR-SSP.
**: Conclusions**A total of 7 investigated samples, 6 of them with anti-Gerbich allo-antibodies, were unambiguously genotyped for their Yus and Gerbich phenotypes using a diagnostic PCR-SSP approach including only four reactions. To our knowledge, this is the first report with a detailed molecular characterization of a “Yus allele”, originally reported together with the “Gerbich allele” in 19892. One other deletional GYPC allele, e.g. encoding the Papua Neuguinean Gerbich phenotype have been reported previously3. An additional Baden-Baden sample is currently under investigation and preliminary results are suggestive of another novel “Yus allele”. Therefore, the provisional ISBT terminology for the alleles encoding the Yus (GE*01.–02) and Gerbich (GE*01.–03) phenotypes will likely need splitting into two alleles each, and revision. Molecular characterization of alleles encoding the Leach phenotype would allow for a fully comprehensive genotyping of Yus, Gerbich and Leach. However, we were unable to obtain samples of the exceptional Leach type, until now.

## Citations

1. Daniels G. Gerbich Blood Group System. In: *Human Blood Groups*. Third. Blackwell Publishing Ltd; 2013:410-426.

2. Colin Y, Le Van Kim C, Tsapis A, et al. Human Erythrocyte Glycophorin C Gene Structure and Rearrangement in Genetic Variants. *J Biol Chem*. 1989;264(7):3773-3780.

3. Scott B, Easteal S. A single-step assay for the Gerbich-negative allele of glycophorin C. *Blood Cells Mol Dis*. 2008;41(1):1-4.